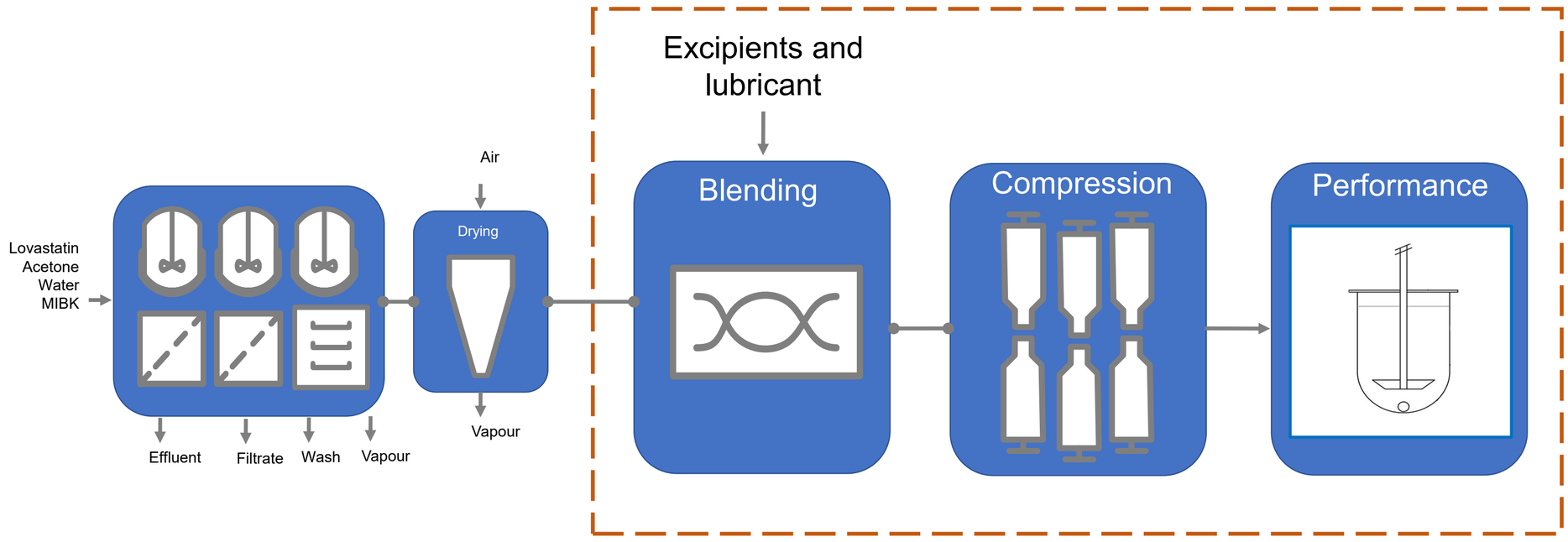
Microfactory – Blend – Compression – Performance test

E. Prasad*, J. Robertson, C. Brown, H. Joliffe, A. Florence and G. Halbert
CMAC Future Manufacturing Research Hub, Strathclyde Institute of Pharmacy and Biomedical Sciences, Glasgow, UK
*for more information contact elke.prasad@strath.ac.uk



Aims and objectives

- API's with acicular habits are commonplace and present processing and handling challenges due to poor flow. This is traditionally addressed by wet granulation processes during formulation. Currently continuous direct compression (CDC) is gaining favour as a simplified formulation and dose formation process. However, poor flow properties limit CDC. This work aims to enable CDC by spherical agglomeration in the primary process and develop underpinning modelling approaches to allow formulations to be explored in-silico (i.e. digital twin)
- Here at CMAC an integrated crystalisation-spherical agglomeration-drying-blending-compression process is being developed (microfactory) to be used to parameterise and develop modelling tools on the g-formulate package
- This work presents some of the activities on the compression component to parameterise and develop a suitable model to enable the process to be explored (i.e. digital twin)

Digital twin

The gFormulate model was parameterised with pure component (Fig. 1) and binary mixtures (Fig. 2) compression data of in terms of tablet tensile strength in the absence of porosity (T_0), bonding capacity (k) and compressibility constant (K) of the Gavi and Reynolds model (2014).

Tensile strength $T = T_0 e^{-k\varepsilon_{tablet}}$

$$\varepsilon_{tablet} = 1 - RD_{tablet}$$

Relative density $RD_{tablet} = RD_{initial} \left(\frac{P}{10^6}\right)^{\frac{1}{K}}$

Volumetric mixing rules

$$\sigma_{T0,mix} = \sum_i \sigma_{T0,i}\phi_i$$

$$k_{b,mix} = \sum_i k_{b,i}\phi_i$$

$$K_{T,mix} = \sum_i K_{T,i}\phi_i$$

Modelling – predictive experimental outcomes (Fig. 2)

- Model fitted reasonably well for single components
- Over-prediction for the binary mixtures: volumetric mixing rules insufficient for complex solid behaviour
- Tablets with a tensile strength > 1.7 MPa are within the 99% confidence interval (○, Fig.2B)

Performance test

Formulated, commercial product releases fastest. Spherical agglomerates release slower than raw material Lovastatin in 20 mg tablets (70% Lactose, 30% Avicel PH-101).

Next steps

Stretch cryst-SA process to provide range of input materials and develop methods to predict model parameters with materials properties
Use pure component parameters to design and optimise targeted experiment to validate model, benchmark and develop digital twin approach

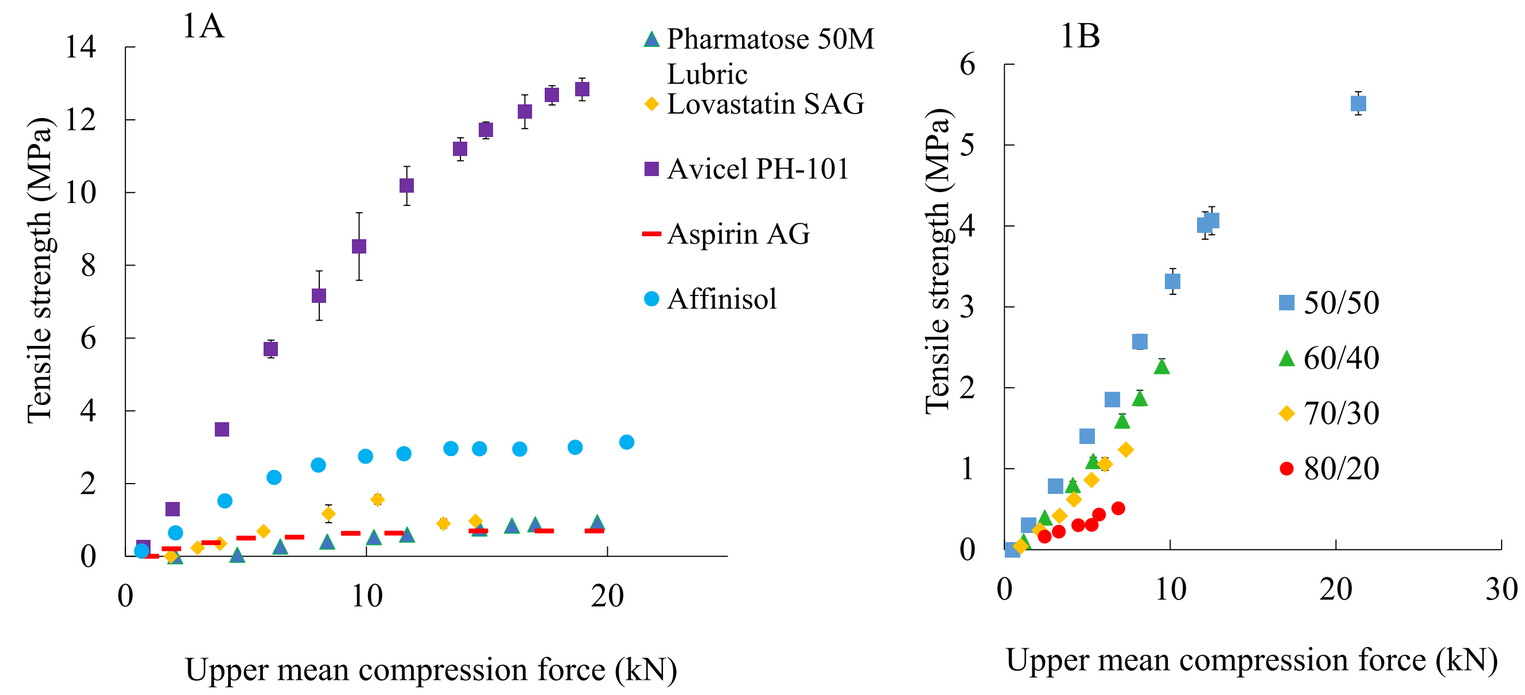


Fig. 1: A) Single component and B) binary mixtures (Pharmatose 50M/Avicel PH-101) compression data.

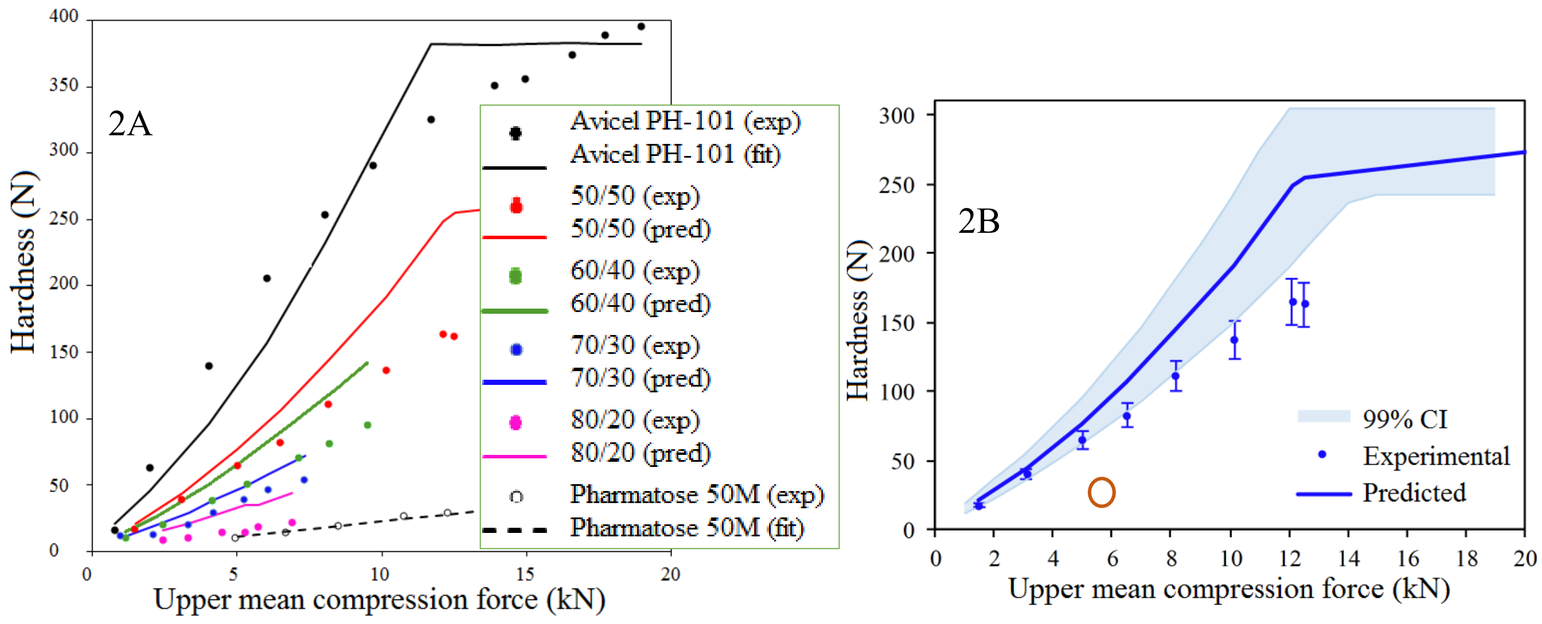


Fig. 2: Predictive experimental outcomes.

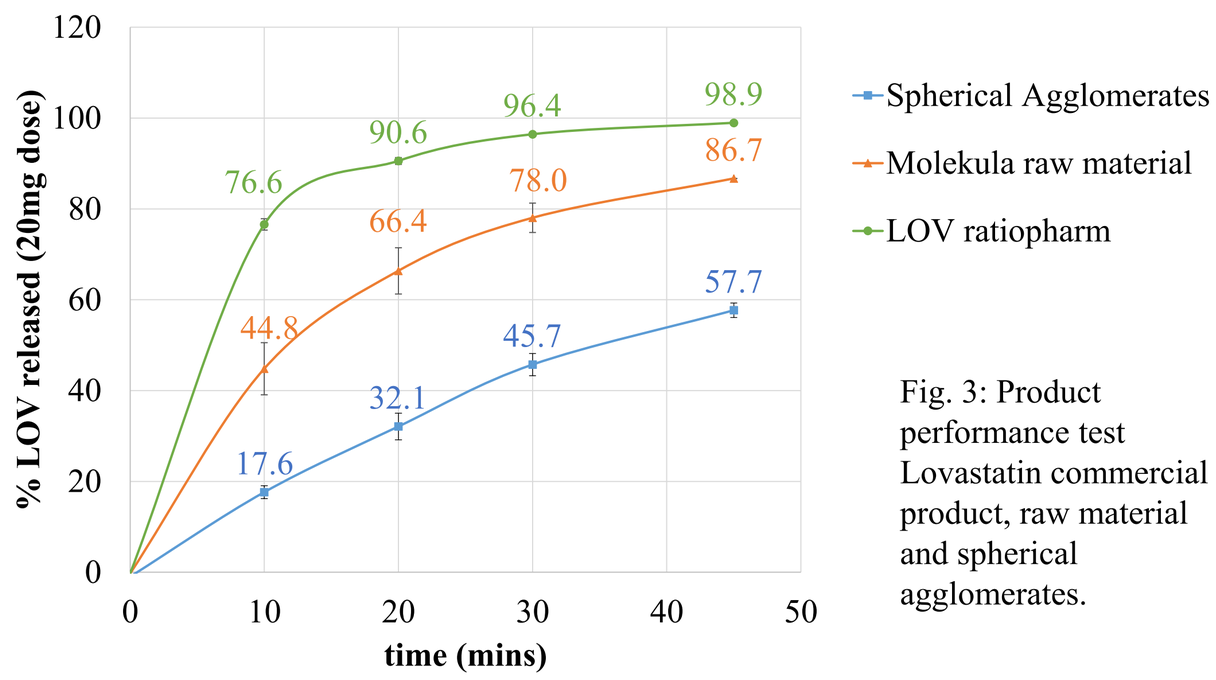


Fig. 3: Product performance test Lovastatin commercial product, raw material and spherical agglomerates.

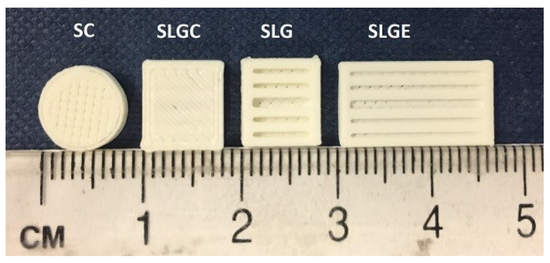
Gavi E., and Reynolds G.K., (2014). System model of a tablet manufacturing process. Comput. Chem. Eng. 71, 130-140.
Leane M., Pitt K., Reynolds G., and Manufacturing Classificstion System Group (2015). A proposal for a drug product Manufacturing Classification System (MCS) for oral solid dosage forms. Pharm. Dev. Technol. 20, 12-21.

Activities - HME – 3D printing process stream

PPA 1 – crystal engineering coupled with polymer processing

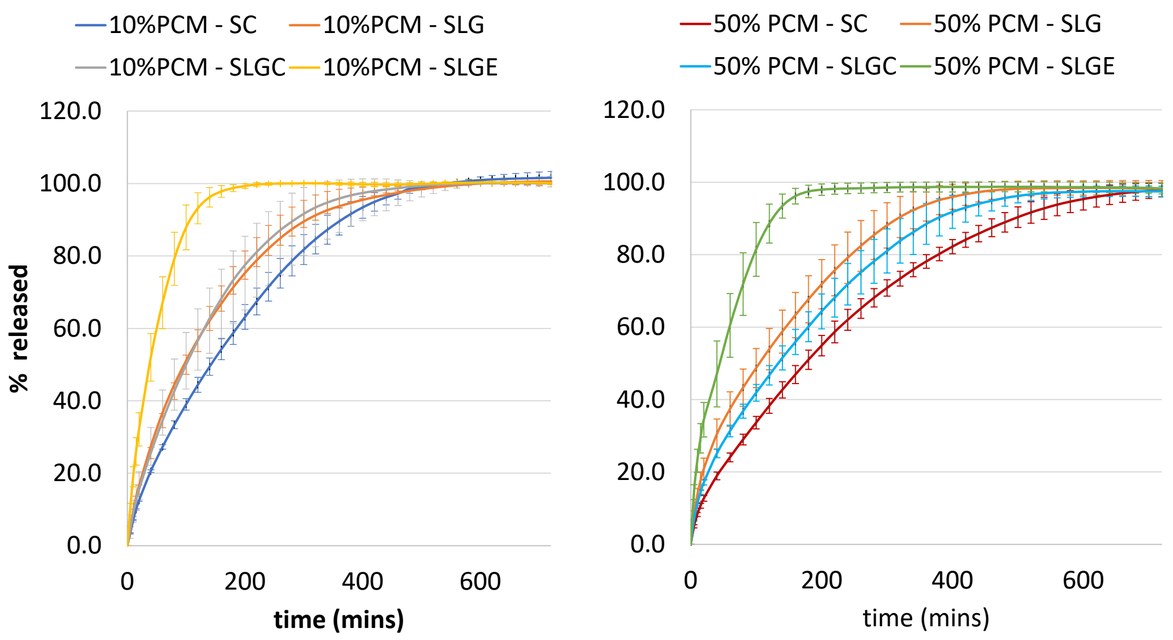
E. Prasad, E. Bordos, A. Anwar, T. M. Islam, J. Robertson, A. Florence and G. Halbert
CMAC Future Manufacturing Research Hub, Strathclyde Institute of Pharmacy and Biomedical Sciences, Glasgow, UK

Tailoring Drug release profile by 3D design of dosage form



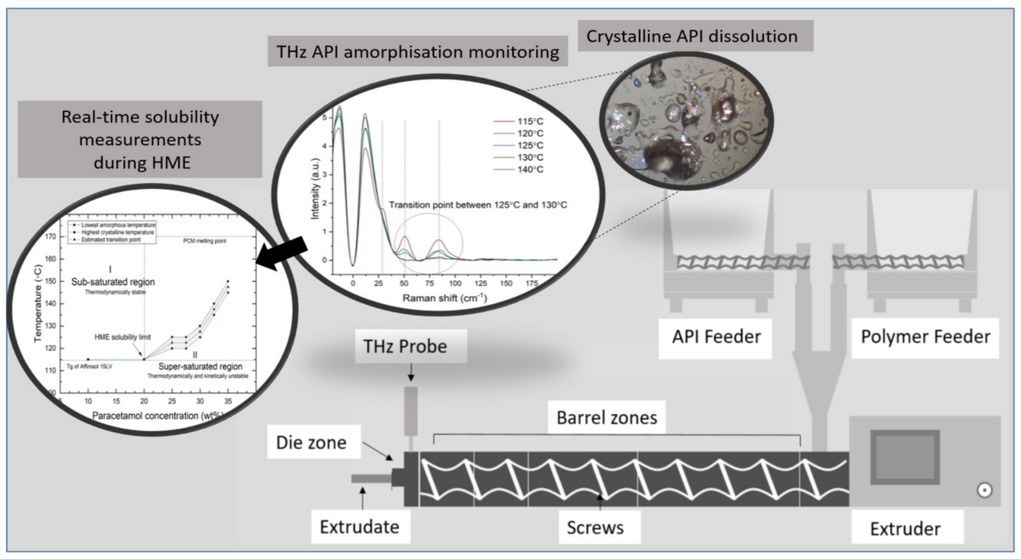
3DP tablet shapes:
SC – solid cylinder, SLGC – slotted grid with cap, SLG – slotted grid, SLGE – slotted grid extended

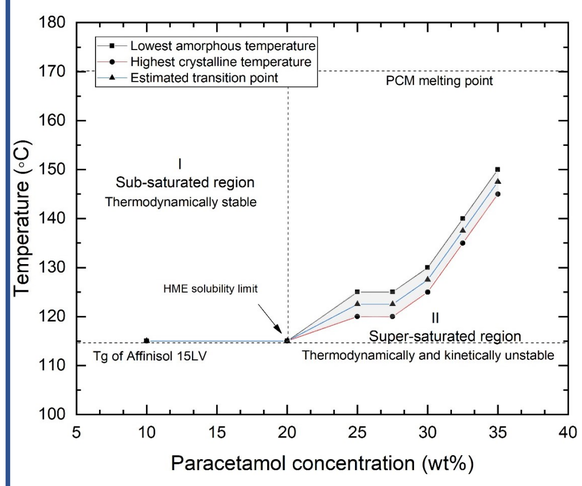
	Volume (mm^3)	Total surface area (mm^2)	Outside Surface Area (mm^2)	Surface Area / Volume (mm^2/mm^3)
SC	157.6	189.6	189.6	1.2
SLGC	160.2	472.0	239.2	1.5
SLG	160.2	391.0	391.0	2.4
SLGE	155.3	515.1	515.1	3.3

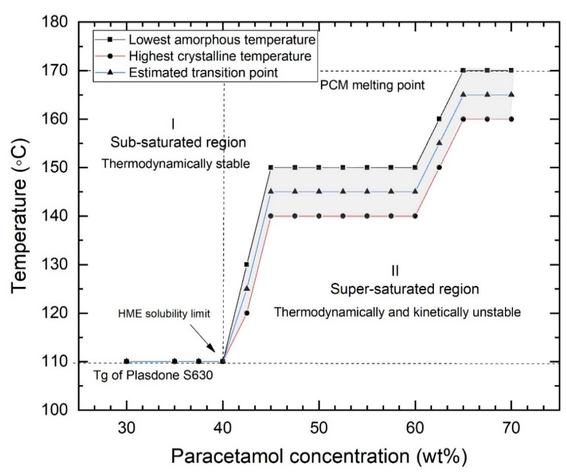


In-vitro drug release profile of 10 and 50 % drug loaded 3DP tablets.

Polymer-Drug Phase Equilibria

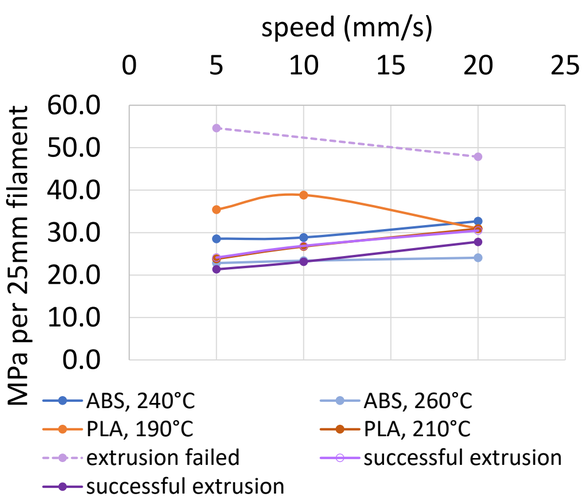


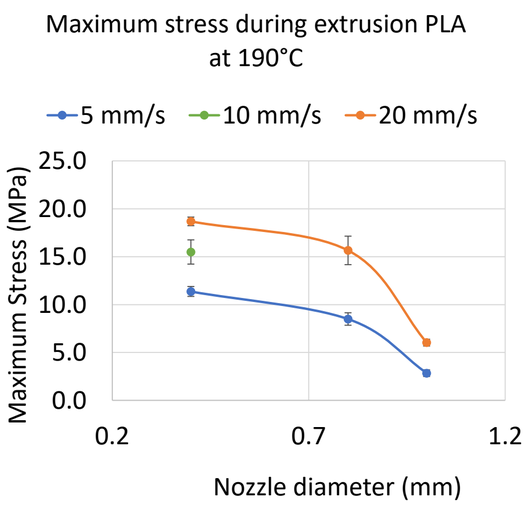




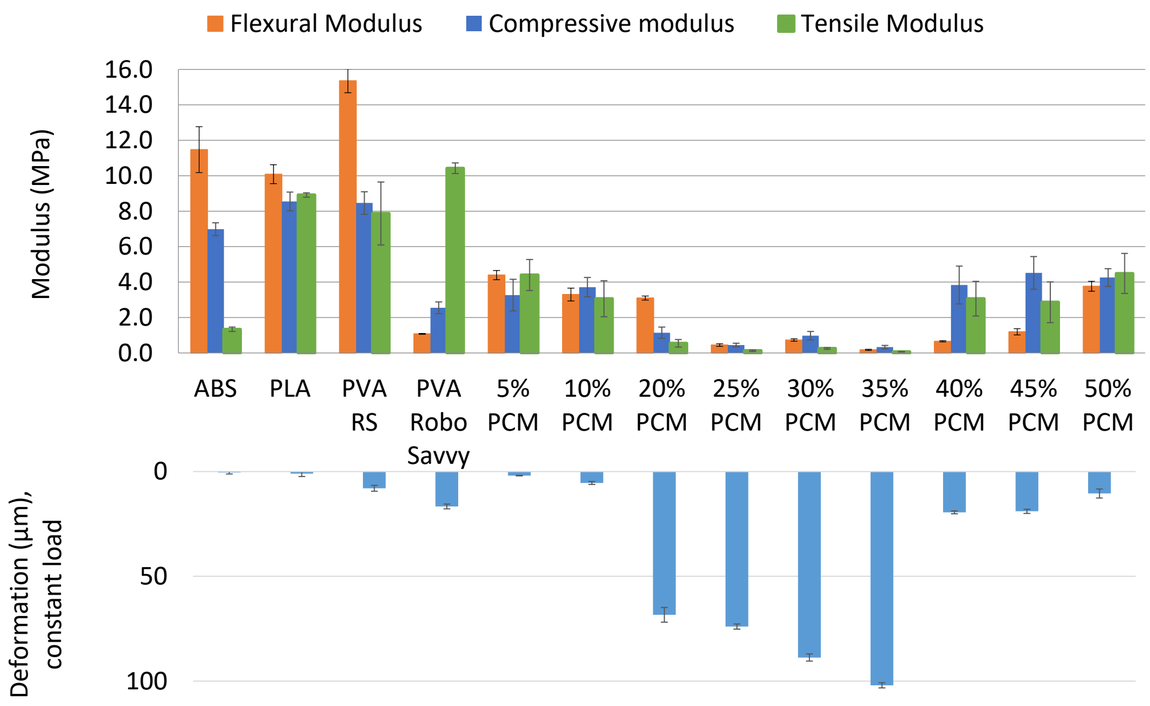
FDM 3D printing filament development

Mechanical properties printing process

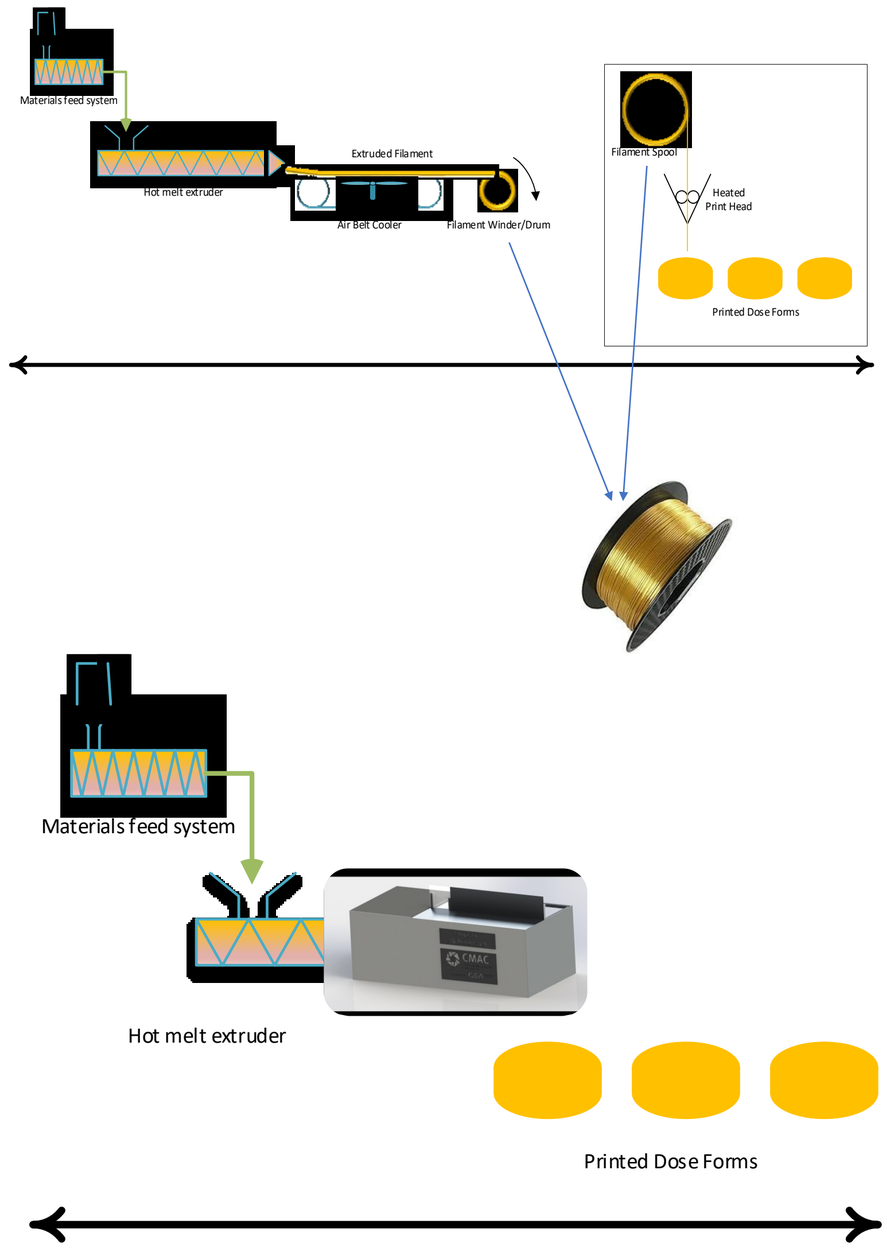




Mechanical properties - FDM filaments



New process platform



EPSRC Engineering and Physical Sciences Research Council · University of Bath · The University of Sheffield · Imperial College London · Loughborough University · gsk · AstraZeneca · Novartis · Bayer · Lilly · Takeda · Roche · Pfizer